

NOV 26 2003

Summary of Safety and Effectiveness Information
Legionella pneumophila IgG/IgM ELISA Test Kit

- I. Trinity Biotech
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Date of preparation: Nov. 20, 2003

II. Description of Device

The *Legionella pneumophila* IgG/IgM ELISA kit is an Enzyme-Linked Immunosorbent Assay (ELISA) for the qualitative detection of total antibodies (IgG and IgM) to *Legionella pneumophila* serogroups 1-6 in serum from patients with clinical suspicion of Legionella Disease.

The *Legionella pneumophila* IgG/IgM ELISA test is an enzyme linked immunosorbent assay to detect IgG/IgM antibodies to legionella. Purified *Legionella pneumophila* antigen (serogroups 1, 2, 3, 4, 5, 6) is attached to a solid phase microtiter well. Diluted test sera is added to each well. If the antibodies are present that recognize the antigen, they will bind to the antigen in the well. After incubation, the wells are washed to remove unbound antibody. An enzyme labeled anti-human IgG/IgM is added to each well. If antibody is present, it will bind to the antibody attached to the antigen on the well. After incubation, the wells are washed to remove unbound conjugate. A substrate solution is added to each well. If enzyme is present, the substrate will undergo a color change. After an incubation period, the reaction is stopped and the color intensity is measured photometrically, producing an indirect measurement of specific antibody in the patient specimen.

III. Predicate Device

The *Legionella pneumophila* IgG/IgM ELISA test is substantially equivalent to BioWhittaker's Legionella STAT test. Equivalence is demonstrated by the following comparative results:

Performance Characteristics

% Agreement Positive and % Agreement Negative

The Trinity Biotech *Legionella pneumophila* IgG/IgM ELISA was evaluated relative to Legionella IFA at two different sites. The first site was a commercial R&D lab located in Maryland. Thirty-three single IFA positive sera, from an outbreak and samples routinely submitted for Legionella testing, were tested. The results of the study are summarized in Table 3.

Table 3
Comparison of Trinity Biotech *Legionella pneumophila* IgG/IgM ELISA and
Legionella IFA
Trinity Biotech *Legionella pneumophila* IgG/IgM ELISA

| | + | eq | - | Total |
|------------------|----|----|---|-------|
| IFA + ≥ 256 | 27 | 3 | 3 | 33 |
| IFA - < 256 | 0 | 0 | 0 | 0 |
| Total | 27 | 3 | 3 | 33 |

% Agreement positive = 27/30 = 90.00% 95% Confidence interval = 79.0% - 100%%
 % Agreement negative = NA 95% Confidence interval = NA

Equivocals were not included in the above calculations.
 The 95% confidence intervals were calculated using the normal method.

Please be advised that “% agreement positive” and “% agreement negative” refer to the comparison of this assay's results to that of a similar assay. There was not an attempt to correlate the assay's results with disease presence or absence. No judgment can be made on the comparison assay's accuracy to predict disease.

The second site was a clinical laboratory in Pennsylvania. Seventy-two prospective serum for *Legionella* testing were tested. The results of the study are summarized in Table 4.

Table 4
Comparison of Trinity Biotech *Legionella pneumophila* IgG/IgM ELISA and
Legionella IFA

Trinity Biotech *Legionella pneumophila* IgG/IgM ELISA

| | + | eq | - | Total |
|------------------|---|----|----|-------|
| IFA + ≥ 256 | 2 | 0 | 0 | 2 |
| IFA - < 256 | 1 | 2 | 67 | 70 |
| Total | 3 | 2 | 67 | 72 |

% Agreement positive = 67/68 = 98.53% 95% Confidence Interval = 95.6% - 100%
 % Agreement negative = 69/70 = 98.57% 95% Confidence Interval = 95.7% - 100%

Equivocals were not included in the above calculations.
 The 95% confidence intervals were calculated using the normal method.

Precision

Seven different sera were assayed at two different sites to determine the precision of the assay. An additional three sera were tested at site 1. Each sera was tested ten times each, on three different days at each of the two study sites. The intra- and inter-assay precision for each site is presented in Tables 5 and 6. The inter-site coefficient of variation (CV) for each serum is presented in Table 7.

Table 5
Trinity Biotech *Legionella pneumophila* IgG/IgM ELISA
Intra- and Inter-Assay Precision
Study 1

| Sera# | Assay 1 (n=10) | | | Assay 2 (n=10) | | | Assay 3 (n=10) | | | Inter-Assay(n=30) | | |
|-------|----------------|-----------|-----------|----------------|-----------|-----------|----------------|-----------|-----------|-------------------|-----------|-----------|
| | <u>X</u> | <u>SD</u> | <u>CV</u> | <u>X</u> | <u>SD</u> | <u>CV</u> | <u>X</u> | <u>SD</u> | <u>CV</u> | <u>X</u> | <u>SD</u> | <u>CV</u> |
| 1 | 3.17 | 0.138 | 4.35% | 3.55 | 0.235 | 6.62% | 3.41 | 0.349 | 10.2% | 3.42 | 0.305 | 8.92% |
| 2 | 2.44 | 0.244 | 10.0% | 2.66 | 0.267 | 10.0% | 2.41 | 0.127 | 5.27% | 2.50 | 0.247 | 9.88% |
| 3 | 2.49 | 0.322 | 12.9% | 2.78 | 0.240 | 8.63% | 2.81 | 0.332 | 11.8% | 2.70 | 0.327 | 12.1% |
| 4 | 1.22 | 0.180 | 14.8% | 1.36 | 0.131 | 9.63% | 1.16 | 0.125 | 10.8% | 1.25 | 0.164 | 13.1% |
| 5 | 0.50 | 0.051 | 10.2% | 0.56 | 0.042 | 7.50% | 0.53 | 0.041 | 7.74% | 0.53 | 0.050 | 9.43% |
| 6 | 0.18 | 0.025 | 13.9% | 0.21 | 0.023 | 11.0% | 0.20 | 0.031 | 15.5% | 0.20 | 0.030 | 15.0% |
| 7 | 0.28 | 0.039 | 13.9% | 0.34 | 0.046 | 13.5% | 0.33 | 0.048 | 14.6% | 0.32 | 0.051 | 15.9% |
| 8 | 1.02 | 0.051 | 5.00% | 1.13 | 0.039 | 3.45% | 1.19 | 0.044 | 3.70% | 1.11 | 0.084 | 7.57% |
| 9 | 0.85 | 0.053 | 6.24% | 0.92 | 0.025 | 2.72% | 0.99 | 0.043 | 4.34% | 0.92 | 0.069 | 7.50% |
| 10 | 0.96 | 0.067 | 6.98% | 1.05 | 0.056 | 5.33% | 1.11 | 0.094 | 8.47% | 1.03 | 0.122 | 11.20% |
| HPC* | | | | | | | | | | 3.64 | 0.402 | 11.05% |
| CAL** | | | | | | | | | | 1.44 | 0.122 | 8.44% |
| LPC* | | | | | | | | | | 1.49 | 0.195 | 13.11% |
| NC* | | | | | | | | | | 0.18 | 0.052 | 28.97% |

* n = 17

** n = 51

Table 6
Trinity Biotech *Legionella pneumophila* IgG/IgM ELISA
Intra- and Inter-Assay Precision
Study 2

| Sera# | Assay 1 (n=10) | | | Assay 2 (n=10) | | | Assay 3 (n=10) | | | Inter-Assay(n=30) | | |
|-------|----------------|-----------|-----------|----------------|-----------|-----------|----------------|-----------|-----------|-------------------|-----------|-----------|
| | <u>X</u> | <u>SD</u> | <u>CV</u> | <u>X</u> | <u>SD</u> | <u>CV</u> | <u>X</u> | <u>SD</u> | <u>CV</u> | <u>X</u> | <u>SD</u> | <u>CV</u> |
| 1 | 2.80 | 0.246 | 8.79% | 2.66 | 0.165 | 6.20% | 3.08 | 0.245 | 7.95% | 2.85 | 0.272 | 9.54% |
| 2 | 3.10 | 0.343 | 11.1% | 3.05 | 0.276 | 9.05% | 3.14 | 0.259 | 8.25% | 3.10 | 0.293 | 9.45% |
| 3 | 3.31 | 0.392 | 11.8% | 3.17 | 0.220 | 6.94% | 3.38 | 0.214 | 6.33% | 3.31 | 0.289 | 8.73% |
| 4 | 1.10 | 0.135 | 12.3% | 1.15 | 0.131 | 11.4% | 1.18 | 0.142 | 12.0% | 1.16 | 0.138 | 11.9% |
| 5 | 0.56 | 0.060 | 10.7% | 0.58 | 0.053 | 9.14% | 0.59 | 0.036 | 6.10% | 0.58 | 0.050 | 8.62% |
| 6 | 0.28 | 0.016 | 5.71% | 0.26 | 0.013 | 5.00% | 0.29 | 0.020 | 6.90% | 0.28 | 0.020 | 7.14% |
| 7 | 0.29 | 0.018 | 6.21% | 0.28 | 0.020 | 7.14% | 0.31 | 0.023 | 7.42% | 0.29 | 0.023 | 7.93% |
| HPC* | | | | | | | | | | 3.16 | 0.092 | 2.91% |
| CAL** | | | | | | | | | | 1.45 | 0.060 | 4.11% |
| LPC* | | | | | | | | | | 1.68 | 0.190 | 11.29% |
| NC* | | | | | | | | | | 0.35 | 0.121 | 34.44% |

* n = 5

** n = 15

Table 7

**Trinity Biotech *Legionella pneumophila* IgG/IgM ELISA
Inter-Site Precision Study
Inter Site (n=60)**

| <u>Sera #</u> | <u>X</u> | <u>SD</u> | <u>CV</u> | <u># positive</u> | <u>#equivocal</u> | <u>#negative</u> |
|----------------------|-----------------|------------------|------------------|--------------------------|--------------------------|-------------------------|
| 1 | 3.13 | 0.406 | 13.0% | 60 | 0 | 0 |
| 2 | 2.80 | 0.403 | 14.4% | 60 | 0 | 0 |
| 3 | 3.00 | 0.431 | 14.4% | 60 | 0 | 0 |
| 4 | 1.21 | 0.158 | 13.1% | 43 | 16 | 1 |
| 5 | 0.56 | 0.055 | 9.82% | 0 | 0 | 60 |
| 6 | 0.24 | 0.046 | 19.2% | 0 | 0 | 60 |
| 7 | 0.30 | 0.040 | 13.3% | 0 | 0 | 60 |
| 8* | 1.11 | 0.084 | 7.57% | 19 | 11 | 0 |
| 9* | 0.92 | 0.069 | 7.50% | 0 | 20 | 10 |
| 10* | 1.03 | 0.122 | 11.20% | 8 | 20 | 2 |
| HPC** | 3.42 | 0.401 | 11.75% | 9 | 0 | 0 |
| CAL*** | 1.45 | 0.069 | 4.77% | 27 | 0 | 0 |
| LPC** | 1.56 | 0.240 | 15.46% | 9 | 0 | 0 |
| NC** | 0.27 | 0.124 | 45.68% | 0 | 0 | 9 |

* n = 30

** n = 9

*** n = 27

X = Mean

SD = Standard Deviation

CV = Coefficient of Variation = $SD/X \times 100$

The methods in NCCLS EP5 were utilized for precision parameters.

IFA Paired Serum Analysis (CDC Panel)

The following information is from a serum panel tested at the Centers for Disease Control (CDC) by IFA and confirmed to be serologically positive for an increase in titer from <1:256 to >1:256. The sera were submitted to CDC for titer confirmation. The results are presented as a means to convey further information on the performance of this assay with a masked serum panel. This does not imply an endorsement of the assay by the CDC.

The panel consisted of thirty-one serum pairs showing a greater than 4-fold increase in IFA titer. Each serum pair was evaluated on the Trinity Biotech *Legionella pneumophila* IgG/IgM ELISA assay to determine a seroconversion in antibody. Twenty nine pairs had a seroconversion, thus giving a % agreement positive of $29/31 = 93.5\%$ in detecting seroconversions.



DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

NOV 26 2003

Ms. Bonnie B. DeJoy
Director, Quality Systems
Trinity Biotech USA
P.O. Box 1059
Jamestown, NY 14702-1059

Re: k033051
Trade/Device Name: *Legionella pneumophila* IgG/IgM ELISA
Regulation Number: 21 CFR 866.3300
Regulation Name: Haemophilus spp. serological reagents
Regulatory Class: Class II
Product Code: MJH
Dated: September 17, 2003
Received: September 29, 2003

Dear Ms. DeJoy:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to such additional controls. Existing major regulations affecting your device can be found in Title 21, Code of Federal Regulations (CFR), Parts 800 to 895. In addition, FDA may publish further announcements concerning your device in the Federal Register.

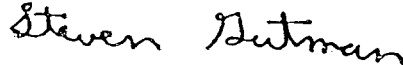
Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); and good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820).

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This letter will allow you to begin marketing your device as described in your Section 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific information about the application of labeling requirements to your device, or questions on the promotion and advertising of your device, please contact the Office of In Vitro Diagnostic Device Evaluation and Safety at (301) 594-3084. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 443-6597 or at its Internet address <http://www.fda.gov/cdrh/dsma/dsmamain.html>.

Sincerely yours,

A handwritten signature in black ink that reads "Steven Gutman". The signature is written in a cursive, slightly slanted style.

Steven I. Gutman, M.D., M.B.A.
Director
Office of *In Vitro* Diagnostic Device
Evaluation and Safety
Center for Devices and
Radiological Health

Enclosure

510(k) Number: K033051

Device Name: Trinity Biotech Captia™ *Legionella pneumophila* IgG/IgM ELISA

Indications For Use: The Trinity Biotech Captia™ *Legionella pneumophila* IgG/IgM ELISA kit is an Enzyme-Linked Immunosorbent Assay (ELISA) for the qualitative detection of total antibodies (IgG and IgM) to serogroups 1-6 in serum from patients with clinical suspicion of Legionella Disease. The assay is not intended to differentiate between the serotypes of *Legionella pneumophila*.

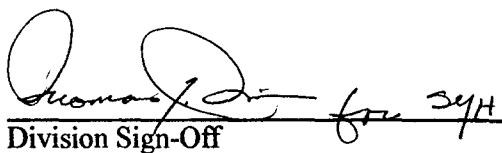
PLEASE DO NOT WRITE BELOW THIS LINE – CONTINUE ON ANOTHER PAGE
IF NEEDED

Concurrence of CDRH, Office of Device Evaluation (ODE)

Prescription Use ☒
(Per 21 CFR 801.109)

OR

Over-The-Counter Use ☐
(Optional Format 1'-2-96)


Division Sign-Off

Office of In Vitro Diagnostic Device
Evaluation and Safety

510(k) K033051